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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/875,349	06/05/2001	John C. Hiserodt	IRVN001DIV	8040

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EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 07/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/875,349	HISERODT ET AL.	
	Examiner	Art Unit	
	Christopher H. Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-50 and 52-82* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-34,36-42,44-50,52,54-64 and 67-82* is/are rejected.

7)☒ Claim(s) *35,43,53,65 and 66* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Re: Hiserodt *et al*

1. The amendment filed 4/13/2005 is acknowledged and entered into the record. Accordingly, claims 1-30, and 51 are canceled without prejudice or disclaimer.

2. Claims 31-50 and 52-82 are pending and examined on the merits.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections Maintained - 35 USC § 103

4. The rejection of claims 31-34,36-40,46-48,50,52,54-57,62,67-72,74-75,78-79, and 82 under 35 USC § 103(a) as being obvious over Kimura *et al* in view of Dick *et al*, and now also in view of Dranoff *et al* (US Patent 5,637,483) is maintained for the reasons of record and newly argued. Applicant argues that the composition taught by Kimura *et al* differs from the instant invention because the authors do not teach or suggest using a gene that encodes the membrane-associated form of M-CSF, but rather directs the skilled artisan to secreted forms of M-CSF. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record.

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When

the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). In the instant case, the cellular composition taught by Kimura *et al* appears to be similar to that instantly claimed. Applicant indicates that the Kimura *et al* fails to teach "membrane-associated" forms of M-CSF. However, it is well known and accepted in the art the mRNA of M-CSF generates both surface/membrane associated and secreted forms of M-CSF protein as evidenced by Cosman *et al* (previously cited). Cosman *et al* further indicate that all forms of M-CSF are at some point membrane associated (see page 22, right col.). Therefore, despite applicant's assertions that Kimura *et al* screened for M-CSF by ELISA does not preclude the fact that the cells express membrane associated forms of M-CSF.

Applicant further differentiates the instant invention from the cited prior art by indicating that the cellular composition claimed is used for treating "*preexisting tumors.*" Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record. A claim containing a "recitation with respect to the manner in which a claimed apparatus is intended to be employed does not differentiate the claimed apparatus from a prior art apparatus" if the prior art apparatus teaches all the structural limitations of the claim. *Ex parte Masham*, 2 USPQ2d 1647 (Bd. Pat. App. & Inter. 1987). In the instant case, the claimed cellular composition appears to the similar to that taught by Kimura *et al* and therefore the means of using the cells for treating "*preexisting tumor*" is not germane to whether or not the prior art is different.

Applicant further argues that a *prima facie* case has not been established because each and every limitation of the claimed invention has not been taught or suggested in the cited art. Specifically, applicant argues that the limitation of the cells being *"inactivated to prevent proliferation"* has not been taught or suggested by either Kimura *et al* or Dick *et al*. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record.

Although it is true that neither Kimura *et al* nor Dick *et al* taught the inactivation of tumor cells prior to administration into a subject, specifically a human subject, it would nonetheless be obvious to do so. This is support by the newly cited reference of Dranoff *et al* (US Patent 5,637,483) who teaches that tumor cell vaccines that are engineered to express GM-CSF can be irradiated or inactivated prior to administration to a subject. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a pharmaceutical composition comprising a human cell that expresses a membrane bound cytokine, wherein the membrane bound cytokine is stably associated with the outer membrane and wherein the cell has been inactivated prior to administration. One of skill in the art would have been motivated to do so because Kimura *et al* taught a cellular composition comprising M-CSF (which has been shown to be membrane associated as evidenced by Cosman *et al*), Dranoff *et al* taught that cellular vaccines engineered to express a cytokine must be irradiated prior to administration, and finally Dick *et al* taught that mouse models are correlative and predictive of human outcomes. Thus one of skill in the art would have expected a reasonable amount of success in making and using an inactivated or

irradiated human cell that expressed a membrane bound cytokine for the purposes of treatment because all of Kimura *et al*, Dick *et al*, and Dranoff *et al* provided sufficient motivation and expectation of success in doing so.

Applicant also argues that the combination of Kimura *et al* in view of Dick *et al* would lead to a differ product, namely a gene vector construct and not the cellular composition as claimed. Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record. These statements are arguments of counsel that have no factual support and are therefore unsubstantiated arguments. Applicant has only provided unsupported conclusions that one of skill would infer from the teachings of Kimura *et al*. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997). In addition, the claims are drawn to the product per se and Kimura *et al* in view of Dick *et al* and Dranoff *et al* teach the claimed product. Applicant additionally argues that the L1210 cells are syngeneic cells based on "virtual" certainty while the instantly claimed invention teaches allogeneic cells. Applicant has not provided factual evidence that the L1210 cells of Kimura *et al* are in fact syngeneic, but only assume that such cells are not allogeneic.

Therefore, for the newly argued reasons and for the reasons already made of record, the rejection of the claims under 35 U.S.C § 103(a) is maintained.

New Arguments

Claim Rejections - 35 USC § 103

5. Claims 31-34,36-42,44-50,52-,54-64, and 68-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Asher *et al* (J. Immunol 1991; 146(9):3227-3234) as evidenced by Karp *et al* (J. Immunol 1992; 149(6):2076-2081) in view of Dick *et al* (previously cited) and Dranoff *et al* (cited above).

a. Asher *et al* as evidenced by Karp *et al* teach a retrovirally transduced tumor cell that expressed TNF alpha that was administered into a subject. Karp *et al* taught that TNF alpha is both membrane bound and secreted (see page 2076). Asher *et al* also taught that at least 5 x 10^6 (specifically, 1 x 10^7) cells were in a unit dose. Moreover, Asher *et al* also taught a method of making the cellular composition comprising the TNFalpha cytokine, by using a retroviral vector under the control of the CMV promoter

b. Asher *et al*, however, do not specifically teach that the cellular composition for administration was irradiated or that the cells used were human cells.

c. These deficiencies are made up by both Dick *et al* and Dranoff *et al* as previously set forth (see record and above).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a pharmaceutical composition comprising irradiated or inactivatd human tumor cells that express a cytokine that is membrane associated, more specifically, an irradiated human tumor cell that expressed membrane associated TNF alpha cytokine. One of skill in the art would have had motivation in doing so because Asher *et al* taught that tumor cells that expressed the TNF alpha was able to regress following in vivo administration, while Dick *et al* taught that mouse

models are predictive and correlative to clinical outcomes. Finally, Dranoff *et al* taught that cells used as cellular vaccines should be irradiated or inactivated prior to administration. Thus one of skill in the art would have found reasonable motivation and expectation of success in using and making a pharmaceutical composition comprising a human cell that comprises a membrane associated cytokine that was irradiated prior to administration so as to prevent proliferation. Moreover, one of skill in the art would have reasonable expectation and success in making the pharmaceutical composition because Asher *et al* taught how the cells can be made using a mouse sarcoma cell line and one of skill in the art could easily apply the same method to a human cell line.

Therefore, for the reasons given above, the claims are obvious.

All other rejections are withdrawn in view of the applicant's amendments and arguments thereto as set forth in a paper filed 4/13/2005.

Conclusion

6. **No claim is allowed.** Claims 35,43,53, and 65-66 are objected to as being dependent upon a rejected base claim.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H. Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen
Art Unit 1642
June 14, 2005